REMARKS

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 11-13 and 15-19 are currently under consideration. Claims 8, 11 and 16 are amended, claim 14 is re-entered for consideration, claims 7, 15 and 20-26 are cancelled, and claims 34-37 are added without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

Claims 8 and 16 are amended to depend from claims 1 and 11, respectively, and claim 11 is amended to incorporate the subject matter of claim 15 and to clarify that the genome of the cell comprises a nucleic acid molecule encoding SV40 T+t. Claims 34-37 relate to the tissue and cell line from which the cells of the invention are derived. Support for the amendment to claim 11 can be found, for example, in Examples 1 and 3 and in the claims as originally filed. Support for new claims 34-37 can be found, for instance on page 3, lines 15-25, and in Examples 1 and 3.

No new matter is added.

It is submitted that the claims herewith are patentably distinct over the prior art, and these claims are in full compliance with the requirements of 35 U.S.C. § 112. The amendments to the claims presented herein are not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply to clarify the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that these amendments should not give rise to any estoppel, as they are not narrowing amendments.

II. THE CLAIM OBJECTIONS ARE OVERCOME

Claims 11, 12, and 15-17 remain objected for being drawn in part to non-elected inventions. This objection is traversed.

Applicants draw attention to the Petition for Withdrawal of Restriction Requirement, which accompanies this Amendment. Therefore, Applicants request that the objection be held in abeyance until the Petition is considered.

III. THE REJECTION UNDER 35 U.S.C. § 103(a) IS OVERCOME

Claims 11-13 and 15-19 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Evan (WO 93/20200) and Givol *et al.* (Cell Growth Differ 5: 419-429, 1994; "Givol"). The rejection is respectfully traversed.

According to the Office Action, Evan relates to cell and cell lines comprising a bcl-2 gene wherein said gene is inserted into a vector; the vector can be integrated and used with host cells from any multicellular organism. The Office Action also alleges that Example 6 in Evan demonstrates cell lines derived from normal tissues, embryonic tissues, lymphoid cells, and haematopoietic cells. Meanwhile, Givol allegedly relates to chicken embryo fibroblasts containing a retroviral vector encoding bcl-2. The Office Action compares these references to the claims of the present invention, which are allegedly drawn to avian cells that are immortalized, but untransformed, comprising an anti-apoptotic bcl-2 gene and optionally the SV40 T+t gene. The Office Action concludes that it would have been obvious to utilize chicken embryo fibroblasts mentioned in Givol as the host cells for the vector mentioned in Evan.

In response, it is initially argued that the combination of Evan and Givol does not lead one of ordinary skill in the art to the present invention. The instant claims, as amended herein, disclose an untransformed, immortalized, avian cell wherein the genome of the cell comprises a nucleic acid molecule encoding SV40 T+t, and wherein the cell contains and expresses a nucleic acid molecule encoding an anti-apoptotic protein. In other words, the cells of the present invention are characterized as being (1) immortalized by introducing the SV40 T+t antigen gene into the cells, mediating stable integration into the genome and stable expression of the transgene; (2) untransformed, as the immortalization does not lead to oncogenic transformation in culture, even at late passages; and (3) contains and expresses an anti-apoptotic protein, which delays the apoptotic process and maintains survival in culture at a confluence state while increasing the cellular density.

Notably, neither Evan nor Givol teach or suggest cells comprising nucleic acids which encode SV40 T+t. Evan does not relate to cells which are immortalized by expression of an oncogene, and Givol in general does not relate to immortalized cells. In fact, Givol is specifically directed to cells that are not immortalized (page 423, right column, last line - page 424, left column, lines 1-3), which teaches away from the present invention. Thus, one skilled in the art would not arrive at the present invention based on the teachings of Evan and Givol.

In addition, it would not be obvious for the skilled artisan to try the present invention as instantly claimed in view of Evan and Givol. Firstly, it was known in the art at the time the present application was filed that immortalization of avian cells is an unlikely achievement. For example, Darnell *et al.* (Molecular Cell Biology, 1960) indicates that "[t]he ease with which transforming stimuli can generate immortal cell lines from cell strains depends on underlying propensity of the cells to spontaneously acquire immortality...Adherent chicken cells are almost never immortalized" (page 967). Further, Guilhot *et al.* (Oncogene 8: 619-624, 1993; attached herein) suggests that "[i]mmortalization by oncogenes from DNA tumor virus has been widely described in the mammalian species...but never in avian species, in which immortalization efficiency is very low" (page 619). Therefore, the skilled artisan would recognize that it is unlikely that avian cells can be immortalized.

Secondly, it was also known in the art that the SV40 large T antigen induces transformation in cells. Guilhot *et al.* indicates that the RB and p53 products are the two most extensively studied anti-oncogene proteins. The adenoviral E1A or E1B products or the E6 or E7 protein of human papillomavirus can inactivate either the RB or p53 product; however, SV40 large T antigen inactivates **both** anti-oncogene products. Hence, the skilled artisan would expect that the SV40 large T antigen will induce tumorigenic characteristics in cells. This is supported by WO 92/10563, which indicates that rabbit epithelial and endothelial cells transfected with a vector expressing SV40 T+t antigen present a tumorigenic phenotype, i.e., has the ability to grow and to form colonies in soft agar culture, and Sompayrac *et al.* (Mol Cell Biol 4: 1661-1663, 1984), which indicates that F111 rat cells transfected by a plasmid coding for SV40 T+t antigen are also tumorigenic (see table 2). Thus, one skilled in the art would expect that expression of SV40 T+t antigen induces tumorigenic characteristics.

With the above in consideration, one skilled in the art would not try to arrive at the immortalized, untransformed cells of the present invention by immortalizing **avian** cells using an a viral oncogene, SV40 large T antigen, that is known to transform cells. Clearly, there is no expectation of success, as such a method contradicts what was known in the art at the time the application was filed. It was indeed surprising that the present inventors succeeded. Thus, it is not obvious to try the present invention in light of the state of the art.

It is further noted that the obviousness analysis must comply with the statutory scheme as explained by the Supreme Court in Graham v. John Deere Co., 383 U.S. 1, 17 (1966), namely,

consideration must be given to: (1) the scope and content of the prior art, (2) the differences between the prior art and the claimed invention, (3) the level of ordinary skill in the pertinent art, and (4) additional evidence, which may serve as indicia of non-obviousness. With this in mind, it is asserted that the present invention fits a specific need in the art. Immortalized, untransformed avian cells can be used for multiplying vaccine viruses, but these cells experience cell apoptosis upon reaching confluence as they cannot grow on top of each other. The incorporation of an apoptotic protein enables immortalized, untransformed cells to survive in a confluence state and increase in cell density. Hence, the present invention fits a specific need for sustaining immortalized, untransformed avian cells that can be used for multiplying vaccine viruses.

Accordingly, it is asserted that the present invention as disclosed in the instant claims is not unpatentable over Evans and Givol. Reconsideration and withdrawal of the Section 103(a) rejection is therefore requested.

CONCLUSION

This application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,

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